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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,880	07/10/2003	Benjamin David Silverman	YOR920030162US1	2640

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EXAMINER	
NEGIN, RUSSELL SCOTT	
ART UNIT	PAPER NUMBER
1631	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/616,880	SILVERMAN, BENJAMIN DAVID	
	Examiner	Art Unit	
	Russell S. Negin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-15 and 17-21* is/are pending in the application.

4a) Of the above claim(s) *10-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-9,14,15 and 17-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Comments

It is acknowledged that claims 6 and 16 are cancelled. Claims 1-5, 7-9, 14-15, and 17-21 are examined in this Office action.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-5, 7-9, 14-15, and 17-21 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

In regards to claims 1-5, 7-9, 14-15, and 17-21, the instant claims are drawn to a biophysical algorithm. A biophysical algorithm is non-statutory unless the claims include a step of physical transformation, or if the claims include a useful, tangible and concrete result. It is important to note, that the claims themselves must include a physical transformation step or a useful, tangible and concrete result in order for the claimed invention to be statutory. It is not sufficient that a physical transformation step or a useful, tangible, and concrete result be asserted in the specification for the claims to be statutory. In the instant claims, there is no step of physical transformation, thus the Examiner must determine if the instant claims include a useful, tangible, and concrete result.

In determining if the instant claims are useful, tangible, and concrete, the Examiner must determine each standard individually. For a claim to be "useful," the claim must produce a result that is specific, substantial, and credible. For a claim to be "tangible," the claim must set forth a practical application of the invention that produces a real-world result. For a claim to be "concrete," the process must have a result that can be substantially repeatable or the process must substantially produce the same result again. Furthermore, the claim must recite a useful, tangible, and concrete result in the claim itself, and the claim must be limited only to statutory embodiments. Thus, if the claim is broader than the statutory embodiments of the claim, the Examiner must reject the claim as non-statutory.

Claims 1-5, 7-9, 14-15, and 17-21 do not produce a tangible result. A tangible result requires that the claim must set forth a practical application to produce a real-world result. This rejection could be overcome by amendment of the claims to recite that a result of the method is outputted to a display or a memory or another computer on a network, or by including a physical transformation.

As stated in MPEP section 2106:

> The tangible requirement does not necessarily mean that a claim must either be tied to a particular machine or apparatus or must operate to change articles or materials to a different state or thing. However, the tangible requirement does require that the claim must recite more than a Sec. 101 judicial exception, in that the process claim must set forth a practical application of that Sec. 101 judicial exception to produce a real-world result. Benson, 409 U.S. at 71-72, 175 USPQ at 676-77 (invention ineligible because had "no substantial practical application."). "[A]n application of a law of nature or mathematical formula to a . . . process may well be deserving of patent protection." Diehr, 450 U.S. at 187, 209 USPQ at 8 (emphasis added); see also Corning, 56 U.S. (15 How.) at 268, 14 L.Ed. 683 ("It is for the discovery or invention of some practical method or means of producing a beneficial result or effect, that a patent is granted . . ."). In other words, the opposite meaning of "tangible" is "abstract."

Claim Rejections - 35 USC § 102

The rejections of claims 1-9 under 35 U.S.C. 102(b) as being anticipated by Silverman [PNAS; April 24, 2001; volume 98, pages 4996-5001] are withdrawn due to amendments made by applicant to the set of claims filed on 17 January 2007.

Claim Rejections - 35 USC § 103

The rejections of claims 14-21 under 35 U.S.C. 103(a) as being unpatentable over Silverman [PNAS; April 24, 2001; volume 98, pages 4996-5001] in view of Michaud [USPAT 4,017,721] are withdrawn due to amendments made by applicant to the set of claims filed on 17 January 2007.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

35 U.S.C. 103 Rejection #1:

Claims 1-5 and 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Silverman [PNAS; April 24, 2001; volume 98, pages 4996-5001] in view of Clarke et al. [PNAS, 1999, volume 96, pages 7232-7237] as evidenced by "Glossary of Medical Terms" [Accessed online on 21 March 2007 from www.uwo.ca/pathol/glossary.html; 22 pages] as evidenced by the definition of "protein tertiary structure" [Accessed online at www.google.com on 21 March 2007].

Claims 1-5 and 7-9 state:

1. A method for calculating a moment of a tertiary protein structure comprising a plurality of residues, the method comprising the steps of:

calculating a centroid of residue centroids; using the centroid of residue centroids as a spatial origin of a global linear hydrophobic moment;

enhancing correlation between residue centroid magnitude and residue solvent accessibility;

defining the global linear hydrophobic moment, wherein each of the residue centroids contributes a magnitude and direction to the global linear hydrophobic moment; and

using the global linear hydrophobic moment to characterize an amphiphilicity of a tertiary protein structure.

2. The method of claim 1, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a distance metric.

3. The method of claim 1, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using an ellipsoidal metric.

4. The method of claim 1, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a solvent accessibility metric.

5. The method of claim 1, wherein the centroid of residue centroids represents a geometric center of the tertiary protein structure.

7. The method of claim 1, wherein the global linear hydrophobic moment characterizes a magnitude of amphiphilicity of the tertiary protein structure.

8. The method of claim 1, wherein the global linear hydrophobic moment characterizes a direction of amphiphilicity of the tertiary protein structure.

9. The method of claim 1, wherein the global linear hydrophobic moment is used to identify functional regions of the tertiary protein structure.

The article of Silverman, "Hydrophobic moments of protein structures: Spatially profiling the distribution," describes how to calculate moments of tertiary protein structures.

In equation [12] on page 4997 of Silverman, r_i is the vector pointing to the centroid of residue *i* while r_c is the vector pointing to the centroid of the entire protein molecule (i.e. the geometric center of the protein).

In equation [13] on page 4998 of Silverman, a first order hydrophobic moment imbalance about the entire protein is written, accounting for hydrophobicity and solvent accessible surface area. Each centroid of every protein residue contributes to this global moment.

In equations [13] and [14] on page 4998 of Silverman, distance metrics, ellipsoidal metrics, and a solvent accessibility are all used to enhance the centroid magnitude.

The global linear hydrophobic moment characterizes the amphiphilicity, and the magnitude and direction of the amphiphilicity of the tertiary protein structure.

Figure 6 on page 5000 of Silverman shows how an arm of the protein can be identified as it falls outside the ellipse characterizing the hydrophobic moment of the protein.

While Silverman demonstrates his technique for a secondary structural component of a protein, Silverman does not show his method for entire proteins.

Clarke et al. shows an isolated single structural element (i.e. a single alpha-helical peptide) comprising an entire protein. The study of Clarke et al., entitled, "The alpha-helix folds on the millisecond time scale" illustrates in Figure 4 at the bottom of column 1 of page 7236 the folding of a single unfolded peptide into a single helix. Clarke et al. explains on page 7232 under "Materials and Methods" that the

compositions of the proteins used to attain the single alpha-helix were polyglutamic acid and polylysine.

While Clarke et al. refers to the molecules in their study as "peptides," peptides are defined in page 16 of the "Glossary of Medical Terms" as "a protein with a small number of amino acids." Consequently, a peptide is a protein.

Even though such proteins as described in Clarke et al. are small, they do not lack structure (i.e. primary, secondary, or tertiary). The definition of "protein tertiary structure" is "the folding of a protein into a 3-D structure." A peptide consisting of an alpha helix is a protein with a three dimensional structure.

It would have been obvious at the time of the instant invention for someone of ordinary skill in the art to modify the secondary structural element of a protein in Silverman by use of an entire protein with a secondary structure that it equivalent to a tertiary structure as shown in Clarke et al. because while Silverman illustrates a method of moment calculation on a portion of a protein, Clarke et al. has the advantage of utilizing proteins comprised in their entireties of single structural units (i.e. the units analyzed by Silverman) for the purpose of better understanding the kinetics of folding of alpha-helices.

35 U.S.C. 103 Rejection #2:

Claims 14-15 and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Silverman in view of Clarke et al. as evidenced by "Glossary of

Medical Terms" as evidenced by the definition of "protein tertiary structure" as applied to claims 1-5 and 7-9 above, in further view of Michaud [USPAT 4,017,721].

14. An apparatus for calculating a moment of a tertiary protein structure comprising a plurality of residues, the apparatus comprising: a memory; and at least one processor operative to: calculate a centroid of residue centroids; use the centroid of residue centroids as a spatial origin of a global linear hydrophobic moment; enhance correlation between residue centroid magnitude and residue solvent accessibility; define the global linear hydrophobic moment, wherein each of the residue centroids contributes a magnitude and direction to the global linear hydrophobic moment; and use the global linear hydrophobic moment to characterize an amphiphilicity of a tertiary protein structure.

15. The apparatus of claim 14, wherein the centroid of the residue centroids represents a geometric center of the tertiary protein structure.

17. The apparatus of claim 14, wherein the global linear hydrophobic moment is used to identify functional regions of the tertiary protein structure.

18. The apparatus of claim 14, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a distance metric.

19. The apparatus of claim 14, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using an ellipsoidal metric.

20. The apparatus of claim 14, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a solvent accessibility metric.

21. An article of manufacture for calculating a moment of a tertiary protein structure comprising a plurality of residues, comprising: a computer-readable medium having computer-readable code embodied thereon, the computer-readable code comprising: a step to calculate a centroid of residue centroids; a step to use the centroid of residue centroids as a spatial origin of a global linear hydrophobic moment; a step to enhance correlation between residue centroid magnitude and residue solvent accessibility; and a step to define the global linear hydrophobic moment, wherein each of the residue centroids contributes a magnitude and direction to the global linear hydrophobic moment.

Silverman in view of Clarke et al. as evidenced by "Glossary of Medical Terms" as evidenced by the definition of "protein tertiary structure" as applied to claims 1-5 and

7-9 above do not teach a computer apparatus of programmable media for performing the claimed analysis.

The patent of Michaud, entitled, "Method and apparatus for determining the position of a body," uses a digital analysis system to calculate a centroid of a body. It is inherent, that in this computer system, there is a computer programmable media to control the computer system.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify Silverman in view of Clarke et al. as evidenced by "Glossary of Medical Terms" as evidenced by the definition of "protein tertiary structure" as applied to claims 1-5 and 7-9 above in further view of Michaud because the invention of Michaud has the advantage of using a computerized system to calculate centroids of objects which provide a more efficient means of calculating physical aspects of objects (i.e. physical aspects of proteins) than calculation by hand.

Response to Arguments

Applicant's arguments filed 17 January 2007 have been fully considered but they are not persuasive.

With regard to the 35 U.S.C. 101 rejection, applicant argues on pages 6-7 of the Remarks of 17 January 2007 that the amendments to the independent claims, "include the tangible result of using the global linear hydrophobic moment to characterize the amphiphilicity of a tertiary protein structure." In response, while this amendment results in a value for a property (the global linear hydrophobic moment), with tangible

consequences when used with proteins, the value of the property itself is a value and is not tangible. As stated in the 35 U.S.C. 101 rejection above, for a claim to pertain to statutory subject matter, it must produce a useful, concrete, and tangible result. In this case, a value of hydrophobicity is a number and is not tangible.

With regard to the anticipatory prior art rejection, applicant argues on page 8 of the Remarks of 17 January 2007, that the Silverman reference teaches "amphiphilicity of a segment of a secondary protein structure," and not the "amphiphilicty of a tertiary protein structure." In this argument, applicant assumes that a tertiary protein structure is always a plurality of secondary protein structures associating to form a domain. In the absence of a definition in the specification of secondary and tertiary structures, the relevant art (i.e. prior art, dictionaries, and glossaries) is consulted to find definitions of terms. Tertiary protein structures are three dimensional structures of proteins. Peptides (or small proteins) can fold into a single three dimensional structure (i.e. a single helix as in Clarke et al.) Consequently, such peptides have tertiary structures that are equivalent to their secondary structures. The art of Silverman is applicable to these peptides.

With regard to the obviousness prior art rejection, applicant argues on pages 9-10 of the Remarks of 17 January 2007, applicant first argues that the patent Michaud does not overcome the alleged deficiencies of the study of Silverman. The arguments pertaining to the Silverman reference are addressed above. Second, applicant states that the Michaud patent in not analogous to the Silverman reference in that the patent of Michaud calculates centroids of figures and not proteins. In response, the Michaud

patent is employed to illustrate a computer system and apparatus in which it is obvious to automate the procedure of Silverman. While the Silverman reference discloses the necessary method for calculating the hydrophobic moment, it does not state that the method must be automated. The patent of Michaud introduces an apparatus accomplishing the related centroid calculation in which the entire procedure is automated, which when applied to the study of Silverman has the advantage of a more accurate, expeditious calculation.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Ram Shukla, Supervisory Patent Examiner, can be reached at (571) 272-0735.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RSN
27 March 2007

3/28/07

28 March 2006
JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER